Ligand Effects

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Inverse Axial-Ligand Effects in the Activation of H_2O_2 and ROOH by an Mn^{III} Corrolazine**

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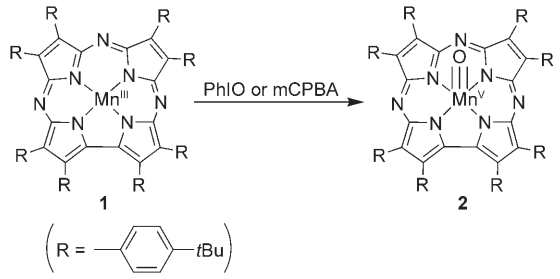
The activation of dioxygen and its two-electron-reduced analogues H_2O_2 and ROOH by both heme- and non-heme-related metal complexes has been the focus of intense efforts because of its relevance to biochemical processes, as well as the potential applications of this chemistry in oxidative catalysis. Heme enzymes such as cytochrome P450, catalases, and peroxidases react with dioxygen and H_2O_2 to give high-valent iron–oxido intermediates such as iron(IV)–oxido π-cation radical ($(porph^{+\cdot})Fe^{IV}=O$), which is presumed to be the critical oxidizing intermediate in cytochrome P450.[1] Delineating the mechanism of formation of these high-valent species, and in particular understanding the O–O-bond cleavage events, remains an important goal. In this regard, many synthetic porphyrin model compounds have been examined to determine the mechanism of O–O-bond cleavage with H_2O_2, ROOH, and organic peracids as oxidants. In these studies, both heterolytic and homolytic cleavage pathways were observed, depending upon the nature of the oxidant and porphyrin employed. However, much remains unknown about what factors (e.g. identity of porphyrin, oxidant, or axial ligand) control the cleavage mechanism.

Herein we describe the reactivity of a manganese(III) corrolazine complex (**1**; Scheme 1) toward H_2O_2 and cumene hydroperoxide (CmOOH). Corrolazines, which are ring-contracted porphyrinoid ligands, have been shown to stabilize



Scheme 1. Synthesis of the stable $Mn^{V}\equiv O$ complex **2**.

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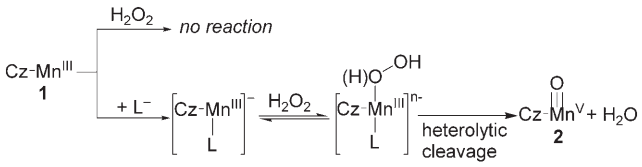
high oxidation states of transition metals.[2] For example, treatment of **1** with the oxidants PhIO or *meta*-chloroperoxybenzoic acid (mCPBA) gives a stable $Mn^{V}{\equiv}O$ complex (**2**; Scheme 1), which can be isolated at room temperature.[3] This system is thus ideally suited to test ideas regarding the mechanism of oxidation by H_2O_2 or ROOH, as the expected high-valent metal–oxido porphyrinoid product can be directly identified. In contrast, when working with conventional porphyrins, one usually has to infer the generation of a high-valent metal–oxido species from indirect observations because of their instability. Herein we report that **1** is indeed capable of activating H_2O_2 and CmOOH, and, moreover, there is a remarkable axial-ligand effect upon these reactions. Also, the axially ligated complex $[Et_4N]^+[(TBP_8Cz)Mn^{III}Cl]^-$ (**3**) was structurally characterized, which to our knowledge is the first example of a structurally characterized anionic corrole species.

We speculated that reaction of **1** with H_2O_2 as the oxidizing agent in place of PhIO or mCPBA should give **2**. Surprisingly, this reaction was a failure; when **1** was dissolved in CH_2Cl_2 or benzene and stirred with excess H_2O_2 (30% aqueous solution) at 23 °C, no **2** was produced, as evidenced by TLC and UV/Vis spectroscopy. However, the coordination of axial ligands to **1** caused a dramatic change in reactivity toward H_2O_2. It has been shown previously by UV/Vis spectroscopy that Cl^- forms a 1:1 complex with **1**.[3c] Addition of H_2O_2 to a solution of **1** and Et_4NCl in CH_2Cl_2 led to an immediate color change from the brown of **1** to the deep green of the $Mn^{V}{\equiv}O$ complex (Scheme 2). Analysis of the



Scheme 2. Activation of H_2O_2 by axially ligated manganese(III) corrolazine.

reaction mixture by UV/Vis spectroscopy and TLC showed that **2** was the major product of this reaction. Isolation after chromatography resulted in a 63% yield of **2**. A likely mechanism for the generation of **2** involves coordination of H_2O_2 to the open site on the Mn center, followed by heterolytic cleavage of the O–O bond ($2e^-$ reduction) to give **2** and OH^-/H_2O. Independent experiments involving addition of Cl^- to **2** show no change in the UV/Vis spectrum, suggesting that once **2** is formed, the Cl^- ion is no longer bound. The strong donation from the triply bonded terminal oxido ligand may discourage binding of negatively charged axial ligands, although we have suggested that a neutral donor (PhIO) may coordinate to **2**.[3b] Some homolytic cleavage may also occur to give a putative Mn^{IV}–O(H) complex that likely rapidly decays.[4] This pathway would account for the less than quantitative yield of **2**.

Definitive proof of axial ligation by Cl^- was obtained by X-ray crystallography (Figure 1).[5] Crystallization of $[Et_4N]^+[(TBP_8Cz)Mn^{III}Cl]^-$ (**3**) was accomplished by vapor diffusion

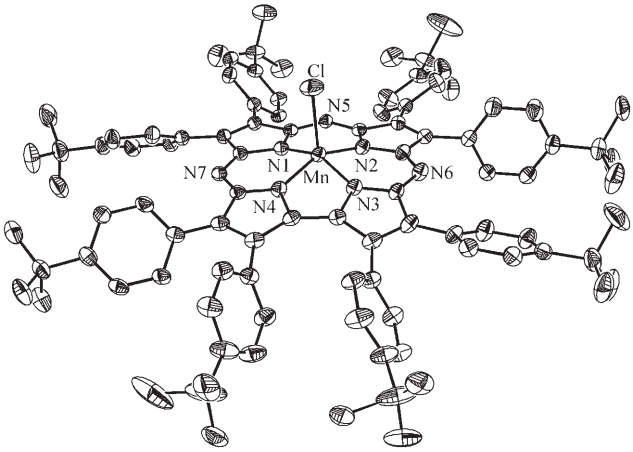


Figure 1. ORTEP diagram of the anion of **3** showing the 50% probability thermal ellipsoids. Hydrogen atoms have been omitted for clarity.

of pentane into a solution of **1**/Et_4NCl in CH_2Cl_2. The Mn ion in **3** is five coordinate with a single axial Cl^- ligand, as expected. The presence of the Et_4N^+ counterion confirms that the complex is negatively charged and the Mn ion is formally in the +3 oxidation state. A UV/Vis spectrum of crystals of **3** redissolved in CH_2Cl_2 matched the spectrum obtained from addition of Et_4NCl to **1** in situ, thus confirming that the complex generated in situ is the same as **3**. The Mn–N and Mn–Cl bond lengths in **3** are normal, and the Mn ion sits significantly further out of the macrocyclic plane (0.6609(7) Å), than in the MeOH adduct $[(TBP_8Cz)Mn^{III}(HOMe)]$[3c] (0.373(2) Å). This large out-of-plane displacement may be due to the steric congestion caused by the large size of the Cl^- ion. The tendency of the corrole to stabilize higher oxidation states appears to make the isolation of negatively charged species rare, whereas corrolazines allow for the isolation of both relatively low- and high-valent complexes.

The strong influence of the axial Cl^- ligand on the H_2O_2 reaction prompted us to examine other potential anionic axial donors. The addition of a series of *para*-substituted arylthiolate donors (p-X-$C_6H_4S^-Na^+$; X = H, OMe, CH_3, Cl, NO_2) had the same general influence as Cl^- on the reactivity of **1** toward H_2O_2: a rapid decay of **1** with concomitant formation of the $Mn^{V}{\equiv}O$ complex. However, a more quantitative comparison made by measuring the rates of reaction of $[\mathbf{1}{-}L]^-$ (L = axial ligand) with H_2O_2 revealed significant differences in the activity of the axial ligands examined. The kinetics were monitored by following the decay of $[\mathbf{1}{-}L]^-$ (absorbance loss at 685 nm; Figure 2). The decay curves were fit to give pseudo-first-order rate constants (k_{obs}), and plots of k_{obs} versus $[H_2O_2]$ showed good linearity; the slopes of these plots yielded the second-order rate constants (k_x''). The observed rate constants include the step involving coordination of H_2O_2 (Scheme 2) and are not a direct measurement of the O–O-bond-cleavage step. However, it is reasonable to assume that the coordination of H_2O_2 is fast and O–O-bond cleavage is the rate-determining step being monitored. Furthermore, the fact that the reaction requires L^- to proceed to any measurable extent suggests that O–O-bond cleavage is

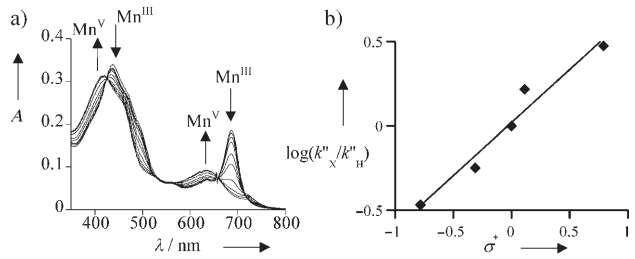
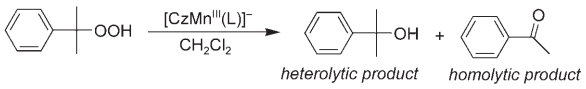


Figure 2. a) Time-dependent UV/Vis spectral changes for **1** + *p*-CH_3-$C_6H_4S^-Na^+$ immediately after addition of H_2O_2. b) Hammett plot for the reaction of $[\mathbf{1}\text{-L}]^- + H_2O_2$ (L = *p*-X-$C_6H_4S^-$).

affected by L^-, because it is unlikely that the coordination of H_2O_2 (or OOH^-) would be strongly enhanced by the formation of $[\mathbf{1}\text{-L}]^-$, a negatively charged complex.

A Hammett analysis of the data (Figure 2) shows that the rate of the H_2O_2 reaction clearly increases with an increase in the electron-withdrawing nature of the arylthiolate ligand ($\rho = 0.63 \pm 0.079$). Assuming this trend arises from an influence on the O–O-bond-cleavage step, this unusual inverse electron demand is opposite to that expected for the normal "push" effect[6] invoked for porphyrin/heme systems such as acylperoxidoiron(III) porphyrins, in which the more electron-donating axial ligand increases the rate of O–O-bond cleavage for both heterolytic and homolytic pathways.[6g,7]

To shed more light on this intriguing axial-ligand effect and obtain a direct measure of the influence of L^- on the mechanism of O–O-bond cleavage, the reaction of cumene hydroperoxide and **1** in the presence of different axial ligands was examined. CmOOH is a useful probe for distinguishing between heterolytic and homolytic cleavage mechanisms, as the former pathway gives 2-phenyl-2-propanol whereas the latter pathway gives acetophenone.[1c,8] The results are summarized in Scheme 3. It is clear that the ratio of



axial ligand:	F^-	Cl^-	Br^-	*p*-NO_2-$C_6H_4S^-$	$C_6H_5S^-$	*p*-MeO-$C_6H_4S^-$
heterol./homol.[a]	2.69	1.15	1.06	2.20	1.78	0.85

[a] mole ratio of alcohol/ketone measured by GC-FID.

Scheme 3. Cleavage pattern of CmOOH + **1** with different axial ligands.

heterolytic versus homolytic cleavage products are strongly influenced by the nature of the axial ligand. There is a dramatic increase in heterolytic cleavage with F^-, which is significantly more electronegative ($F^-_{EN} = 4.2$) than Cl^- ($Cl^-_{EN} = 2.8$) or Br^- ($Br^-_{EN} = 2.7$). Similarly, heterolytic cleavage increases with the electron-withdrawing nature of the *para* substituent of the arylthiolate donors. These trends are in good agreement with the inverse electron demand observed for the reaction of **1** + H_2O_2 in the presence of axial ligands.

The axial-ligand effect described herein is in stark contrast to the normal push effect observed for both metalloporphyrins and hemoproteins. Interestingly, recent work by Nam et al. describes a similar, unusual inverse electronic effect for certain iron porphyrins, in particular, when H_2O_2 or ROOH is employed as the oxidant.[9] This latter effect appears to be operative when either the electronic properties of the porphyrin ligand itself, or the coordinated axial ligands are varied, and a rationale for these observations has been offered.[9b] We have clearly established that the electronic properties of anionic axial ligands bound to a manganese(III) corrolazine have a strong influence on the mechanism of O–O-bond cleavage for peroxide-type oxidants. Furthermore, this influence is exactly opposite to the expected trend from a classical push effect. In future work it would be of interest to determine if neutral donors (e.g. pyridine, imidazole) show similar trends, and if the origin of these effects can be discerned. These observations should help in understanding the mechanism of O–O-bond cleavage in porphyrinoid systems of both synthetic and biological origin. Moreover, the insights gained regarding the activation of oxidants such as hydrogen peroxide may lead to the design of practical corrolazine-based catalysts that can utilize the highly desirable terminal oxidant H_2O_2, or perhaps even O_2 itself.

Experimental Section

2: H_2O_2 (30% aq, 0.0125 mL, 0.11 mmol) was added to a solution of **1** (15 mg, 11 μmol) and Et_4NCl (2.2 mg, 13 μmol) in CH_2Cl_2, and the reaction mixture was stirred for 1 h. During this time the color changed from the dark brown of **1** to the deep forest green of **2**. The crude product was purified by chromatography (silica gel, CH_2Cl_2) to give **2** as a green solid. Yield: 9.5 mg, (63%).

3: Under aerobic conditions, **1** (5 mg, 3.55 μmol) and Et_4NCl (0.7 mg, 4.26 μmol) were dissolved in CH_2Cl_2 (5 mL) and allowed to stand. Vapor diffusion of pentane into this solution over 7 days yielded green-brown crystals of **3**, which were isolated by decantation and air-dried. UV/Vis spectroscopy (CH_2Cl_2): $\lambda_{max} = 435, 480, 635$ nm. Elemental analysis (%) calcd for $C_{110}H_{138}Cl_3MnN_8$ (**3**·CH_2Cl_2·pentane 1733.6 g mol^{-1}): C 76.21, H, 8.02, N, 6.46; found: C 75.53, H, 8.42, N, 5.95.

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[5] Data collection for **3**·$(CH_2Cl_2)_{2.5}$: $T = 110$ K, $M_r = 1788.82$, crystal dimensions: $0.29 \times 0.24 \times 0.20$ mm^3, triclinic ($P\bar{1}$), $a = 15.2032(13)$, $b = 18.1447(16)$, $c = 21.632(2)$ Å, $\alpha = 69.001(9)$, $\beta = 87.647(8)$, $\gamma = 69.974(8)°$, $V = 5211.4(8)$ Å^3, $Z = 2$, $\rho = 1.140$ g cm^{-3}, $(Mo_{K\alpha}) = 0.328$ mm^{-1}, $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å), $2\theta_{max} = 52.74°$. X-ray diffraction intensities were collected on an Xcalibur3 diffractometer; total number of reflections 104404, independent reflections 21023 [$R_{int} = 0.0277$]. Final R factors [$I > 2\sigma(I)$]: $R1 = 0.0712$, w$R2 = 0.2124$, $GoF = 1.071$. Data were collected, integrated, and corrected for absorption and interframe scaling with the CrysAlis Pro suite of programs (Oxford Diffraction). The structure was solved and refined with the SHELXTL (6.10) suite of programs (G. Sheldrick, Bruker XRD, Madison, WI, **2000**). The structure was solved by using direct methods and completed by subsequent difference Fourier syntheses and refined by full matrix least-squares procedures on F^2. All non-hydrogen atoms were refined with anisotropic displacement coefficients; several additional disordered solvent molecules could not be modeled appropriately. Electronic contributions from these molecules were removed via SQUEEZE (Platon). H atoms were placed in calculated positions and refined by using a riding group model. CCDC-616545 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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